

REMARKS

Claims 1-90 are pending. Claims 48-51, 54, 57, 59-61, 66-69, 72, 75, and 78-80 are under examination. Claims 48, 50, 51, 66, 68 and 69 have been amended. Support for the amendments can be found throughout the specification and the claims as filed. Accordingly, these amendments do not raise an issue of new matter and entry thereof is respectfully requested.

Submitted herewith is a Sequence Listing in compliance with 37 C.F.R. § 1.821-1.825. Sequence Listing pages 1 through 2 are submitted herewith containing Sequences 1 through 4, formatted in accordance with the conventions set forth by PatentIn. Entry of these pages is respectfully requested.

Applicants appreciate Examiner Steele's reconsideration and rejoinder of Groups VI and VII.

Applicants bring to the Examiner's attention that an Information Disclosure Statement is being filed today by first class mail.

Regarding the Sequence Listing

In the Office Action, a Sequence Listing has been requested to be filed. Submitted herewith is a Sequence Listing in compliance with 37 C.F.R. § 1.821-1.825. The specification has also been amended to recite SEQ ID NOS corresponding to the Sequence Listing submitted herewith. Applicants respectfully submit that the requirements of 37 C.F.R. § 1.821-1.825 have been satisfied.

Regarding the Objection to the Claims

In the Office Action, it is indicated that claims 48-51, 54, 57 and 59-61 are objected to for the phrase "second ligand in the bound, wherein." Claim 48 has been amended as requested by the Examiner to recite "bound complex." Accordingly, Applicants respectfully request that the objection to the claims be withdrawn.

Rejection Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 48-51, 54, 57, 59-61, 66-69, 72, 75 and 78-80 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite is respectfully traversed. Applicants respectfully submit that the claims are clear and definite.

With respect to the assertion that there is insufficient antecedent basis for the phrase “second ligand homologs,” Applicants respectfully disagree and point out that the first recitation of “second ligand homolog” occurs in step (d) of claim 48. Nevertheless, claims 48, 50, 51, 68 and 69 have been amended to recite “homologs of said second ligand.”

The Office Action indicates that claim 66 is considered to be indefinite for the recitation of “homologs” in line 2 of step (e), which is asserted to lack antecedent basis. Applicants respectfully disagree but nevertheless have amended claim 66 to recite “homologs of said second ligand identified in step (d).”

The Office Action additionally indicates that the term “fragment” as recited in claims 48, 50, 66 and 68 is considered to render the claims indefinite and to be a relative term. Applicants respectfully disagree but nevertheless have amended the claims reciting “fragment thereof” to further recite “fragment thereof that binds to the common ligand binding site of said protein.”

The Office Action further indicates that the term “homolog” is considered to render the claims indefinite and to be a relative term. Applicants respectfully disagree and submit that one skilled in the art would readily understand the meaning of the term “homolog” based on the teachings in the specification and what was well known to those skilled in the art. In particular, the specification teaches that a “homolog” is a molecule or moiety of a molecule that has a similar structure in comparison to a reference molecule or moiety (page 22, paragraph [063]). Furthermore, the claims have been amended to recite “homolog of said second ligand,” and Applicants respectfully submit that this phrase is clear to one skilled in the art.

Claims 48 and 66 are asserted to be indefinite in the Office Action for the term “isotope-edited” pertaining to NOESY, which is asserted to be a relative term. Applicants respectfully disagree and submit that the term “isotope-edited” is a term of art in the field of NMR spectroscopy. The specification teaches, for example, that a signal can be selectively detected

when an isotope filter or relaxation filter is used such as described in Cavanaugh et al., Protein NMR Spectroscopy: Principles and Practice Chapter 7, Academic Press, San Diego (1996), and the specification further describes examples of isotope-filtered or edited NMR methods (see paragraph [0117]). Such methods include isotope-filtered experiments that detect ^1H signals attached to $^{12}\text{C}/^{14}\text{N}$ nuclei and remove $^{13}\text{C}/^{15}\text{N}$ -attached ^1H signals, and isotope-edited (isotope-separated) experiments that detect ^1H signals attached to $^{13}\text{C}/^{15}\text{N}$ nuclei and remove $^{12}\text{C}/^{14}\text{N}$ -attached ^1H signals for selective observation of interactions between $^{13}\text{C}/^{15}\text{N}$ isotope-labeled and unlabeled molecules. Commonly used isotope edited or filtered methods include 2D X-edited TOCSY, or the analogs 3D TOCSY-HMQC and 2D TOCSY-HSQC; 2D X-edited NOESY, or the analogs 3D-NOESY-HMQC and 3D NOESY-HSQC, and 3D and 4D HMQC-NOESY-HMQC. Such methods can employ a variety of well-known filters to allow the study of intramolecule NOES between a ligand and a protein. Exemplary filters include $^{13}\text{C}(\omega_2)$ -filtered/ $^{12}\text{C}(\omega_1)$ -selected experiments and $^{13}\text{C}(\omega_1)$ -filtered/ $^{12}\text{C}(\omega_2)$ -selected experiments (see specification paragraph [0117]). Thus, Applicants respectfully submit that term “isotope-edited” is clear to one skilled in the art based on the teachings in the specification and what was well known in the art.

The term “linked” or “linkage” is asserted in the Office Action to render claims 48, 50, 51, 66, 68 and 69 indefinite and to be a relative term. Applicants respectfully disagree and submit that the term “link” or linkage” is clear to one skilled in the art. Nevertheless, the claims have been amended to recite “covalent” link or linkage.

Applicants respectfully submit that that the claims are clear and definite. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 102

The rejection of claims 48-51, 54, 57, 59-61, 66-69, 72, 75 and 78-80 under 35 U.S.C. § 102(b) as allegedly anticipated by Sem, U.S. Patent No. 6,333,149, is respectfully traversed. Applicants respectfully submit that the claimed methods are novel over Sem.

Claim 48, as amended, is directed to a method for obtaining a focused library of candidate binding compounds for a protein family, wherein the members of the protein family

bind a common ligand. The method includes the steps of (a) providing a ligand-probe having an antenna moiety, wherein the ligand-probe binds to the common ligand binding site of a protein, wherein the protein is a member of the protein family; (b) providing a sample comprising the protein, the ligand-probe and a second ligand under conditions wherein the ligand-probe, the second ligand and the protein form a bound complex; (c) detecting a subset of magnetization transfer signals between the antenna moiety of the ligand-probe and the second ligand in the bound complex, wherein the signals are obtained from an isotope-edited NOESY spectrum of the sample, thereby determining that the antenna moiety and second ligand are proximal in the bound complex; and (d) obtaining a population of candidate binding compounds comprising the ligand-probe, or a fragment thereof that binds to the common ligand binding site of said protein, covalently linked to one of a plurality of homologs of the second ligand, whereby the population contains binding compounds that bind to members of the protein family.

Claim 66, as amended, is directed to a method for obtaining a focused library of candidate binding compounds, wherein the members of the protein family bind a common ligand. The method includes the steps of (a) providing a ligand-probe having an antenna moiety, wherein the ligand-probe binds to the common ligand binding site of a protein, wherein the protein is a member of the protein family; (b) providing a plurality of samples comprising the protein and the ligand-probe under conditions wherein the ligand-probe and the protein form a bound complex, wherein the protein is a member of a family of proteins that bind a common ligand; (c) assaying a population of candidate second ligands for the ability to transfer magnetization to the antenna moiety of the ligand-probe in a sample from the plurality, wherein the ability to transfer magnetization is assessed by determining a subset of magnetization signals of a an isotope-edited NOESY spectrum of the sample; (d) identifying, from the population of candidate second ligands, a second ligand that transfers magnetization to the antenna moiety of the ligand-probe, thereby determining that the two ligands are proximal to each other in a ternary bound complex with the protein; and (e) obtaining a population of candidate binding compounds comprising the ligand-probe, or a fragment thereof that binds to the common ligand binding site of said protein, covalently linked to one of a plurality of homologs of the second ligand identified in step (d), whereby the population of candidate binding compounds contains binding compounds that bind to members of the protein family.

Applicants respectfully submit that Sem provides no teaching of a method for obtaining a focused library of candidate binding compounds for a protein family, as in Applicant's claimed methods. Therefore, Applicants respectfully submit that Sem cannot anticipate the claims. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Double Patenting Rejections

The rejection of claims 48-51, 54, 57, 59-61, 66-69, 72, 75 and 78-80 for obviousness-type double patenting as allegedly being unpatentable over claims 1-33 of U.S. Patent No. 6,333,149 is respectfully traversed. Applicants respectfully request that this rejection be held in abeyance until there is an indication of allowable subject matter.

The rejection of claims 48-51, 54, 57, 59-61, 66-69, 72, 75 and 78-80 for obviousness-type double patenting as allegedly being unpatentable over claims 1-62 of U.S. Patent No. 6,620,589 is respectfully traversed. Applicants respectfully request that this rejection be held in abeyance until there is an indication of allowable subject matter.

The rejection of claims 48-51, 54, 57, 59-61, 66-69, 72, 75 and 78-80 for obviousness-type double patenting as allegedly being unpatentable over claims 1-160 of U.S. Patent No. 6,797,460 is respectfully traversed. Applicants respectfully request that this rejection be held in abeyance until there is an indication of allowable subject matter.

The provisional rejection of claims 48-51, 54, 57, 59-61, 66-69, 72, 75 and 78-80 for obviousness-type double patenting as allegedly being unpatentable over claims 59-100 of co-pending application serial No. 10/884,181 is respectfully traversed. Applicants respectfully request that this rejection be held in abeyance until there is an indication of allowable subject matter.

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

10/799,934

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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